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TREATMENT PLANNING AND DOSE CALCULATION IN RADIATION ONCOLOGY

Third Edition

by

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PERGAMON PRESS
New York Oxford Toronto Sydney Paris Frankfurt

Pergamon Press Offices:

U.S.A.	Pergamon Press Inc., Maxwell House, Fairview Park, Elmsford, New York 10523, U.S.A.
U.K.	Pergamon Press Ltd., Headington Hill Hall, Oxford OX3 0BW, England
CANADA	Pergamon Press Canada Ltd., Suite 104, 150 Consumers Road, Willowdale, Ontario M2J 1P9, Canada
AUSTRALIA	Pergamon Press (Aust.) Pty. Ltd., P.O. Box 544, Potts Point, NSW 2011, Australia
FRANCE	Pergamon Press SARL, 24 rue des Ecoles, 75240 Paris, Cedex 05, France
FEDERAL REPUBLIC OF GERMANY	Pergamon Press GmbH, Hammerweg 6, 6242 Kronberg/Taunus, Federal Republic of Germany

Library of Congress Cataloging in Publication Data

Bentel, Gunilla C. (Gunilla Carleson), 1936-

Treatment planning and dose calculation in radiation oncology.

Bibliography: p.
Includes index.
1. Cancer--Radiotherapy. 2. Radiation--Dosage.
I. Nelson, Charles E. II. Noell, K. Thomas.
III. Title. [DNLM: 1. Radiometry. 2. Radiotherapy dosage. 3. Neoplasms--Radiotherapy. QZ 269 B475t]
RC271.R3B46 1982 616.99'40642 82-15001
ISBN 0-08-027176-6
ISBN 0-08-027175-8 (pbk.)

Second Printing 1985

Printed in Great Britain by A. Wheaton & Co. Ltd., Exeter

PREFACE TO THE THIRD EDITION

The first edition of this text was intended as a guide for trainees in radiation oncology at Duke University. However, requests for copies from other institutions were substantial and necessitated another printing. The third edition has been substantially revised to include more general treatment planning methods.

The discussion of radiation physics has been enlarged and a new section on brachytherapy has been added.

The rapid development of new procedures and sophisticated equipment in radiation oncology makes it impossible to include all of the latest techniques. The target localization techniques and treatment plans presented are intended as guides only.

It is the authors' hope that this edition is sufficiently general to serve a wide audience in the radiation oncology community. It is our hope that this edition will provide a practical guide to treatment planning for technologists, dosimetrists, physicists, radiation oncologists, and other health care professionals.

G.C.B.
C.E.N.
K.T.N.

ACKNOWLEDGEMENTS

Our thanks for collaboration and assistance go to the staff of the Radiation Physics and Radiation Oncology Divisions of the Department of Radiology of Duke University Medical Center, with special thanks to Fearghus O'Foghludha, Ph.D., Dan Miller, Ph.D., Arnold Herskovic, M.D., and Susan Wiseman, R.T.(T.). Thanks are extended to Mr. Brady Lambert for his work on the photographs and to Ms. Rose Boyd and Ms. Connie Faison for typing the manuscript.

INTRODUCTION

Cancer is often cured. Patients, families and many health professionals still too often assume that the diagnosis of a malignant tumor is a death sentence. Cure is the total and permanent eradication of a disease, and cancer is cured with everyday regularity by surgical and radiotherapeutic means, and several types of malignancy are now curable with chemotherapy. This is a singular achievement. Of mankind's many serious illnesses, cure is now only achieved in the treatment of infectious and neoplastic diseases.

Of course, not every patient with cancer is curable. However, the large majority receiving radiation therapy of palliative intent obtain some symptomatic relief. Thus, while a career in radiation oncology can have its bad moments, it is not depressing. It is rather marvelous that radiation therapy works so well and so often.

Ionizing radiations must be used wisely, with full understanding of their injurious as well as their therapeutic potentials. In this volume we offer treatment methods and technical guides as models of contemporary radiation therapy. These models should be modified for each individual patient to yield a best fit to the disease being treated and the radiation sources employed.

CAUTION

The treatment plans described in this text are suggested field arrangements and treatment techniques only. No responsibility is accepted for application of these plans without consideration of a particular patient's contour or target volume, and of the beam data particular to the individual therapy machine.

All radiation doses stated assume fractionation at 180-200 rad per day in a continuous course of 5 treatments per week unless otherwise indicated.

CHAPTER 1

ELEMENTS OF CLINICAL RADIATION ONCOLOGY

The thoughtful application of ionizing radiations requires consideration of their effects on normal tissues and of the type of tumor and its extent. The volume to be treated and intended radiation doses are then determined. Treatment planning explores the choices of technique; the best method is executed. Finally, periodic evaluation of the patient after treatment is essential (Fig. 1.1).

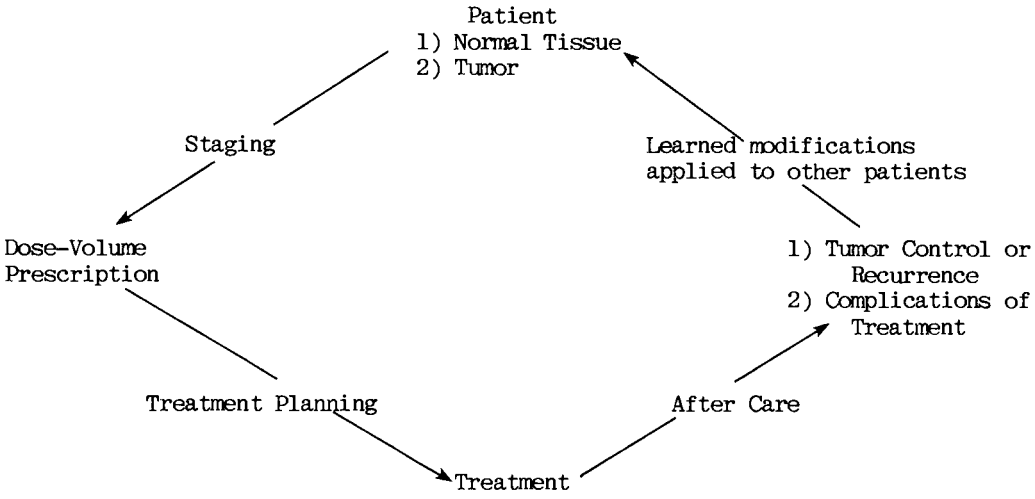

Fig. 1.1. The process of radiation oncology.

Normal Tissue and Organ Effects of Irradiation

Injury of mature tissues and organs. Every region of human anatomy has dose limiting tissues and organs which are essential for the patient's survival in a functional state. Symptomatic functional impairment is of principal concern and subtle, microscopic, cellular or tissue alterations are not further considered in this work, except to note that low dose gonadal irradiation may have profound teratogenic effects while the irradiated parent remains free of significant organic injury.

The lens of the eye is perhaps the most radiosensitive structure. A single dose of 200 rad may cause development of a cataract in this previously crystal-clear structure, with secondary visual impairment. The tissue probably most tolerant of irradiation is the smooth muscle of the uterus and uterine cervix which routinely accepts doses of the order of 10000 rad. Vitally important organs such as kidney, lung, liver, heart and brain lie between these two dose extremes (Tables 1.1-1.3). While the human organism has been graced with a number of spare parts, permitting normal or near normal survival despite the loss of a kidney or lung, for example, it is important to understand that radiation damage of such a spare part may have late and life-threatening consequences. Radiation pneumonitis and fibrosis, for example, can result in profoundly disabling shortness of breath, and the damaged lung may be the focus of recurrent infections (pneumonia, bronchiectasis). Unilateral radiation nephropathy may be followed by secondary hypertension.

TABLE 1.1

Organs in which radiation lesions are fatal or result in severe morbidity

Organ	Injury	$TD_{5/5}$	$TD_{50/5}$	Whole or Partial Organ (Field Size or Length)
Bone marrow	aplasia, pancytopenia	250 3000	450 4000	whole segmental
Liver	acute and chronic hepatitis	2500 1500	4000 2000	whole whole strip
Stomach	perforation, ulcer, hemorrhage	4500	5500	100 cm^2
Intestine	ulcer, perforation, hemorrhage	4500 5000	5500 6500	400 cm^2 100 cm^2
Brain	infarction, necrosis	6000	7000	whole
Spinal cord	infarction, necrosis	4500	5500	10 cm
Heart	pericarditis and pancarditis	4500 7000	5500 8000	60% 25%
Lung	acute and chronic pneumonitis	3000 1500	3500 2500	100 cm^2 whole
Kidney	acute and chronic nephrosclerosis	1500 2000	2000 2500	whole (strip) whole
Fetus	death	200	400	whole

$TD_{5/5}$: tissue dose associated with a 5% injury rate within 5 years.
$TD_{50/5}$: tissue dose associated with a 50% injury rate within 5 years.

Modified from RADIATION BIOLOGY AND RADIATION PATHOLOGY SYLLABUS, Rubin P. (Ed), American College of Radiology, Chicago, Illinois, 1975.

TABLE 1.2

Organs in which radiation lesions result in moderate to mild morbidity

Organ	Injury	$TD_{5/5}$	$TD_{50/5}$	Whole or Partial Organ (Field Size or Length)
Oral cavity and pharynx	ulceration, mucositis	6000	7500	50 cm^2
Skin	acute and chronic dermatitis	5500	7000	100 cm^2
Esophagus	esophagitis, ulceration	6000	7500	75 cm^2
Rectum	ulcer, stricture	6000	8000	100 cm^2
Salivary glands	xerostomia	5000	7000	50 cm^2
Bladder	contracture	6000	8000	whole
Ureters	stricture	7500	10000	5-10 cm
Testes	sterilization	100	200	whole
Ovary	sterilization	200-300	625-1200	whole
Growing cartilage, bone (child)	growth arrest, dwarfing	1000 1000	3000 3000	whole 10 cm^2
Mature cartilage, bone (adult)	necrosis, fracture, sclerosis	6000 6000	10000 10000	whole 10 cm^2
Eye				
a) Retina		5500	7000	whole
b) Cornea		5000	>6000	whole
c) Lens		500	1200	whole or part
Endocrine glands				
a) Thyroid	hypothyroidism	4500	15000	whole
b) Adrenal	hypoadrenalism	>6000	---	whole
c) Pituitary	hypopituitarism	4500	20000-30000	whole
Peripheral nerves	neuritis	6000	10000	10 cm
Ear				
a) Middle	serous otitis	5000	7000	whole
b) Vestibular	Meniere's syndrome	6000	7000	whole

$TD_{5/5}$: tissue dose associated with a 5% injury rate within 5 years.
$TD_{50/5}$: tissue dose associated with a 50% injury rate within 5 years.

Modified from RADIATION BIOLOGY AND RADIATION PATHOLOGY SYLLABUS, Rubin P. (Ed), American College of Radiology, Chicago, Illinois, 1975.

TABLE 1.3

Organs in which radiation lesions result in mild transient, reversible effects or in no morbidity

Organ	Injury	$TD_{5/5}$	$TD_{50/5}$	Whole or Partial Organ (Field Size or Length)
Muscle (child)	atrophy	2000-3000	4000-5000	whole
Muscle (adult)	fibrosis	6000	8000	whole
Lymph nodes and lymphatics	atrophy, sclerosis	5000	>7000	whole node
Large arteries and veins	sclerosis	>8000	>10000	10 cm^2
Articular cartilage	none	>50000	>500000	joint surface (mm^2)
Uterus	necrosis, perforation	>10000	>20000	whole
Vagina	ulcer, fistula	9000	>10000	whole
Breast (child)	no development	1000	1500	whole
Breast (adult)	atrophy, necrosis	>5000	>10000	whole

$TD_{5/5}$: tissue dose associated with a 5% injury rate within 5 years.
$TD_{50/5}$: tissue dose associated with a 50% injury rate within 5 years.

Modified from RADIATION BIOLOGY AND RADIATION PATHOLOGY SYLLABUS, Rubin P. (Ed), American College of Radiology, Chicago, Illinois, 1975.

Serious adverse effects of irradiation may not be manifested for several years after treatment. Therefore, those patients who survive a usually fatal illness such as carcinoma of the lung may also survive long enough to develop radiation myelopathy. The fact that adverse effects of therapeutic irradiation may be delayed in making their appearance emphasizes the need for follow-up.

Specific discussion of dose limiting normal structures is found in Chapter 7.

Impaired Tissue and Organ Development

Patients who receive radiation therapy before reaching physical maturity are subjected to a host of adverse outcomes because irradiation often limits subsequent normal tissue or organ development. This is most frequently observed after irradiation of skeletal muscles and bones, which do not develop as fully as their non-irradiated symmetrical counterparts. A shortened extremity of limited muscular development may result from the irradiation of an extremity in childhood, and kyphoscoliosis is a potential sequel of irradiation of a segment of the spine.

The effects of irradiating normal tissues in the young are further considered in Chapter 7.

Radiation Tumorigenesis

It is increasingly recognized that irradiation may cause the formation of both benign and malignant tumors. This is particularly true when irradiation is administered in childhood, but applies to adults as well. Perhaps the best example is the thyroid gland. Incidental irradiation of the neck for a variety of benign conditions, especially in childhood, is associated with the development of a variety of thyroid abnormalities 5 to 35 years later. Twenty-seven percent of 1056 irradiated patients subsequently evaluated at Michael Reese Hospital in Chicago were found to have thyroid abnormalities, and 7% of the total group were found to have thyroid carcinomas (Favus 1976). Osteosarcoma and fibrosarcoma, both highly malignant tumors, are now known to occasionally follow radiotherapy for retinoblastomas and pituitary tumors. Breast cancer may follow irradiation of the chest, and all leukemias, except chronic lymphocytic leukemia, developed with increased incidence in Japanese atomic bomb survivors.

The potential adverse effects of radiation therapy must receive adequate recognition when treatment of any patient is contemplated. There is no treatment in medicine which is absolutely devoid of risk, and risks must be carefully weighed against potential benefits for every patient prior to initiation of therapy, including radiation therapy.

Staging

Treatment of any illness is based on an understanding of its natural history. The extent of a neoplastic process determines the prognosis. Assessment of the primary tumor (T), the regional lymph nodes (N), and distant metastases (M) allows classification of the disease for prognostic and therapeutic purposes. This process is known as staging. Simply put, at diagnosis the malignancy may be at an early, intermediate, or late stage of its natural history.

The American Joint Committee for Cancer Staging and End-Results Reporting uses the TNM system; for each tumor site, TNM combinations are grouped in stages, of which there are usually four. For lung cancer, for example, stage I includes these TNM combinations: TIS NO MO, T1 NO MO, T1 N1 MO, and T2 NO MO. TIS indicates carcinoma in situ; T1 a primary tumor 3 cm or less in diameter, and T2 a larger tumor. NO and MO signify absence of demonstrable regional lymph node and distant metastases, respectively; and N1 signifies involvement of the first echelon of regional nodes (American Joint Committee 1978, p 60). The survival prospects for these seemingly rather different TNM combinations are roughly similar, permitting a stage I classification for each.

Several staging systems exist. This complicates the interpretation of treatment results. Ideally, each patient's record should contain a statement of which staging system was used to determine the designated stage of the disease.

There are also several levels of staging: clinical, surgical, and pathological. Preoperative radiotherapy utilizes clinical (non-surgical) staging. The intent of preoperative radiotherapy is to improve tumor resectability and reduce the viability of tumor cells which may be spread through the operative site. In contrast, the results of surgical staging can only be incorporated in the treatment plan when irradiation is given postoperatively.

The Dose-Volume Prescription

Once the tumor is staged, and hence prognosis is determined, treatment will generally proceed with either palliative or curative intent. The dose-volume prescription incorporates many factors: tumor dose, normal tissue tolerance limits, available equipment parameters, co-existing medical problems, and dose

fractionation factors, with due consideration of the patient's psychologic and socio-economic status. A further discussion is beyond the scope of this text since this covers the entire field of radiation oncology.

Treatment

Optimal treatment requires a conscientious daily effort to minimize any variation from the selected treatment plan. Daily precision in patient positioning and beam direction is facilitated by a variety of techniques and tools, from cardboard cutouts to laser side lights. As Perez has stated, "We must now concentrate on defining the optimal doses for each tumor...that yield the highest cure rate with few severe sequelae and without jeopardizing the subsequent useful and comfortable life of the patient. This leads us to the concept of dose optimization, for which high quality treatment planning and reproducible treatment techniques are crucial" (emphasis added) (Perez 1977).

A final comment on treatment: it is generally advisable to treat each field each day, with few exceptions.

After Care

Periodic evaluation of most patients after radiotherapy is an important component of radiation oncology, especially after the higher doses of curative intent. The radiation oncologist should be better at determining whether new medical problems are due to radiotherapy than other medical specialists. Radiotherapy remains poorly understood by many physicians, nurses, and other health professionals, who incorrectly attribute a variety of new symptoms to prior radiotherapy; this occasionally reaches bizarre proportions. Compounding the problem, patients and referring physicians often view follow-up visits to the radiation oncologist as inconvenient and an unnecessary expense. Yet, the expense is generally modest and demonstration that the patient is free of both tumor and serious adverse radiation effects is important feedback. When adverse effects of radiotherapy appear, the radiation oncologist should be instrumental in determining appropriate treatment.

Evaluation of a recurrent tumor by the radiation oncologist is essential: is salvage therapy possible, and if so, by what method? How should the radiation therapy of future patients be modified?

The Cost Effectiveness of Radiation Therapy

In 1978, all medical care costs totalled $139 billion in the United States, or 8.6% of the Gross National Product. Total cancer care costs then were estimated as about $20 billion, with radiotherapy accounting for only 2.5%, or $500 million, of total cancer care. In their report, the Subcommittee on CT Scanning and Radiation Therapy of the Committee on Radiation Oncology Studies indicated that direct care costs of each failed cancer patient were $36,000, compared to a $12,000 cost for each cured cancer patient. On the average, then, failure to cure costs an additional $24,000 per patient. Each 1% increase in cure is estimated to save $90 million in direct cost ($24,000 x 375,000 cancer deaths per year x 0.01) (Stewart 1978). In 1978 dollars, a 5.5% increase in cure rates ($90 million x 5.5 = $495 million) would entirely offset the direct costs of radiation therapy.

Sick patients are usually too sick to work. It has been estimated that cancer patients unable to work lose $10 billion a year in earnings (Oncology Times 1981).

Of course, not all patients are irradiated with curative intent, but the message should be clear: relatively modest increases in cure rates yield important economic results. It is our hope and expectation that the cost of thoughtful treatment planning and precise treatment will be more than offset by improvement in tumor control and in normal tissue damage.

CHAPTER 2

RADIATION PHYSICS

Physics, in particular radiation physics, has been an integral part of radiology since its inception. The very essence of both diagnostic and therapeutic radiology is rooted in the physical interactions between radiation, both electromagnetic and particle, and the atoms that constitute all of matter. These interactions are now well understood and the intent of this brief review is not to shed any new light on this subject. Rather, it is hoped that a review of the production, interaction and measurement of radiation will serve as an anchor in the fundamentals of radiation physics necessary to understand their practical consequences in dose calculations.

Production of Radiation

Radiation, whether electromagnetic in character such as light, or particulate, such as electrons, can be thought of as simply a means of transferring energy from a source to an object some distance away. While the interaction of radiation with tissue is the proper end point of a discussion of radiation therapy dose calculations, the discussion begins with the production aspect. Furthermore, the development of the various machines presently in use in the modern radiation oncology department followed a straightforward path from simple to complex, e.g. the low energy x-ray tubes of Coolidge (Coolidge 1913) were developed before the principle of the linear electron accelerator of Wideroe (Wideroe 1928) was conceived. The discussion below follows this historical development.

X-ray Tubes

Fundamental to all of the means of production of radiation is some device or machine which can increase the energy of the particle, e.g. an electron, to a level such that when it returns this kinetic energy to the environment, it does so by producing both heat and 'light' e.g. radiation. One method of accomplishing this is to provide a source of many electrons, a large voltage difference through which the electrons can be accelerated, thereby gaining energy and, finally, a target for the accelerated electrons to hit and produce heat (kinetic energy of atoms of the target) and radiation via the conversion of some of their kinetic energy (energy of motion) to short wave length radiant energy, or x-rays. Since electrons lose energy rapidly to air via ionization of air molecules, i.e. producing positive and negative ions through collisions, the acceleration process must take place in a vacuum. Furthermore, since most of the

energy released by these fast moving electrons results in the production of heat, the x-ray target must be cooled in some manner. These requirements are all satisfied by the x-ray 'tube', normally an evacuated glass housing which provides a vacuum, suitable electrical insulation between the anode and cathode and a means for cooling the anode. The major difference between diagnostic x-rays and low energy x-rays used for therapy is the x-ray flux or the total amount of radiation produced per unit time. This difference leads to several different engineering features (higher filament current, more efficient anode cooling, etc.) between the two areas but the radiation physics is identical.

The x-ray target, or anode, is bombarded by a large number of energetic electrons during x-ray production. The number of possible different ways the electron can interact with the target atom is large and depends on the electron energy. However, from a practical point of view, these interactions can be limited to essentially two types: elastic and inelastic collisions.

Elastic, billiard-ball type collisions between the electron and the atom's electron cloud or nucleus result in lowering the incident electron's energy by transferring some of this energy to another electron or atom in the form of kinetic energy of the electron or atom. This kinetic energy on an atomic scale shows up macroscopically as heat.

An inelastic collision between an electron and the nucleus of the atom results in a lower energy electron and an electromagnetic wave (x-ray) which carries away this kinetic energy in the form of an x-ray photon. This 'braking radiation' (bremsstrahlung) accounts for almost all of the x-ray production from an x-ray tube. The amount of x-rays produced depends strongly on the initial electron energy, rising with higher kV. The direction of the x-rays produced is also dependent on the electron energy; the x-ray beam becomes more forward directed at higher kV. The production of x- rays by bremsstrahlung is the source of x-rays from linear electron accelerators and betatrons. The primary difference between these devices and the x-ray tube, man's first particle accelerator, is the energy of the electron.

Superficial Therapy Units

Radiation therapy x-ray equipment in the 60-140 kV range is used for superficial therapy. The maximum absorbed dose or energy deposited in a mass of tissue occupying a small volume is produced on the surface with a very rapid fall off of dose with increasing depth. This equipment produces a large amount of very soft (low energy) x-rays which can produce a severe skin reaction. To prevent this, these units are usually equipped with one or several filters through which the x-ray beam must pass. These filters, commonly aluminum sheets, selectively remove this very soft radiation and are placed immediately adjacent to the x-ray tube.

Orthovoltage Therapy Units

Radiation therapy x-ray equipment operating in the 250-500 kV range is referred to as orthovoltage equipment. Again, except for the engineering requirements necessary to produce and apply such high voltages, the physics is identical. Reasonable tissue penetration of the resultant x-ray beam is achieved with this equipment, which also must be operated with filters to reduce the soft x-rays. The maximum dose is achieved on the skin as with the superficial units; however, the additional penetrating power of these 'hard' x-rays allows the treatment of lesions located within a few centimeters of the surface without delivering excessive dose to the skin.

Van de Graaffs, Betatrons and Linear Accelerators

The ability to produce and maintain voltage differences greater than approximately 300 kV using the techniques and equipment of the standard x-ray machines is limited. The production of 500 kV to 1,000,000 volts (1 MV) must be accomplished with other means. The first particle accelerator to reach such high voltages was developed by R. J. Van de Graaff in 1931 (Van de Graaff 1931). This type of accelerator can accelerate electrons up to 3 MeV (million electron volts, a unit of energy). These electrons are directed towards a water cooled target (anode) and produce a very high radiation field in the same direction as the electron beam, via bremsstrahlung. The amount of soft (low energy) radiation produced by such a high energy electron beam is very large but since the x-rays must penetrate the anode or target, usually gold or copper, the target itself serves as a 'beam-hardening' filter and removes the low energy x-rays from the beam. The Van de Graaff accelerator requires an insulating gas to prevent high voltage arcing within its structure. As a consequence, Van de Graaff accelerators in clinical use normally are encased in a large metal tank which is supported from the ceiling. This tank contains the insulating gas under high pressure.

The betatron, perfected by Kerst in 1941 (Kerst 1941), uses a time varying magnetic field to produce very high energy electrons in a relatively compact arrangement. Very high voltages are avoided completely by accelerating the electron beam in a small circle via a time varying magnetic field arranged to be perpendicular to this circle. The resulting electron beam is no longer continuous but is a series of pulses of electrons separated by periods of no beam. The x-ray output of the betatron is large, in the direction of the electron beam and, of course, pulsed. This is the first of the 'pulsed' accelerators used for radiation therapy. By maintaining a large quantity of electrons in each pulse, substantial outputs are easily obtained.

The first linear accelerator was designed by Wideroe in 1928 for the acceleration of heavy, positively charged particles. It was not until the development of very high frequency oscillators during World War II for radar applications that electron linear accelerators were feasible. Bunches of electrons are injected into an electromagnetic wave guide and 'ride the crest' of this travelling wave to voltages up to 20 MV or more. Standing wave guides, operating in a somewhat similar manner, can also be used. These linear electron accelerators provide a pulsed source of very high energy electrons which are directed at a target to produce very high outputs of x-rays in the forward direction.

The primary advantage of the high energy x-ray beams that are produced by these devices is the increased ability of the beam to penetrate to greater depths of tissue. In addition, the depth of maximum dose is no longer at the surface but is below the surface. The higher the energy of the x-ray beam, the further below the surface this maximum is located. The consequence of this location of the maximum dose is the reduced dose at the skin surface which leads to the skin sparing effect, wherein the dose to the skin surface is less than the dose to the underlying tissue.

The primary x-ray beam from these 'supervoltage' therapy units is extremely forward peaked, so much so in fact, that custom designed 'flattening filters' must be built in order to provide a flat, symmetric beam on the patient. These filters selectively attenuate the primary beam to produce a uniform beam over a large area (up to 40 x 40 cm in some accelerators). Figure 2.1 shows a flattening filter for a 16 MV x-ray beam.

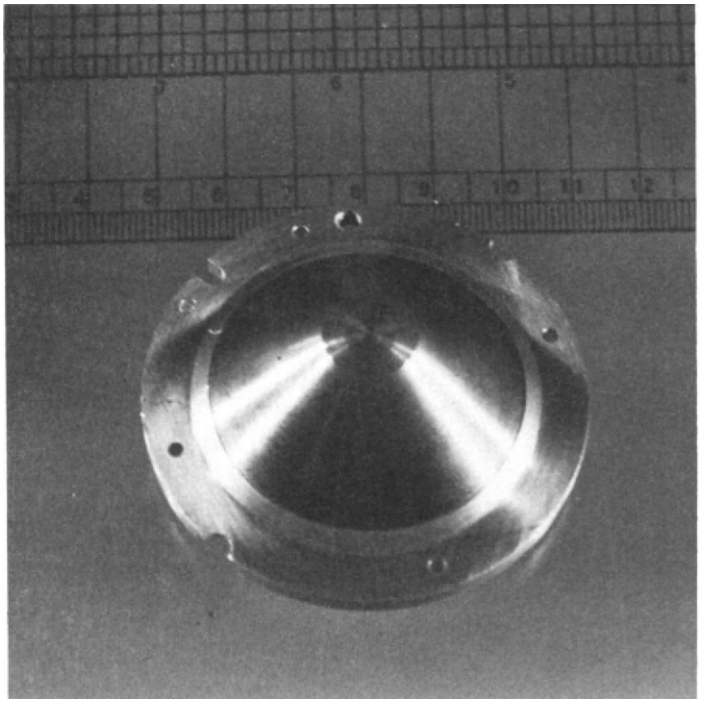

Fig. 2.1. Beam flattening filter for a 16 MV photon beam

The energy of the electrons is such in both betatrons and linear accelerators that the electrons can be used directly for patient treatment. By simply removing the flattening filter, done automatically in modern machines, and allowing the electron beam (at reduced current) to penetrate the 'window' separating the accelerator vacuum from the outside environment, direct electron radiation is possible. This electron beam is so narrow that it must be scanned across the patient's skin in some accelerators. In others, it is scattered with the aid of a 'scattering foil' and an electron applicator or cone. This provides a broadening of the beam to treat a limited volume of tissue. The electron beam produces its maximum dose near the patient's skin so that there is little skin sparing. However, the dose fall off with depth is very sharp with electrons and this allows the sparing of organs deep within the treatment field.

Van de Graaff accelerators, betatrons and linear accelerators are much more complicated pieces of equipment than x-ray tubes. They require constant dose verification and continued maintenance. However, the advantages they bring to patient care are substantial and they have provided the treatment of choice in many institutions.

The cyclotron (Lawrence 1932), while not used routinely for radiation therapy, is a machine used to accelerate heavy charged particles, other than electrons, to very high energy. This is accomplished by the combination of a fixed magnetic field which constrains the charged particles to move in a circle perpendicular to the magnetic field. An alternating high frequency voltage is applied to two hollow electrodes which accelerate the particle a small amount